REMARKS/ARGUMENTS

Claims 1-21 are pending in the application. Claims 22-23 were canceled.

Claims 1 and 10 have been amended. Claims 12-21 have been canceled without prejudice. Claims 24-26 have been added. Entry of the amendment, reconsideration of the rejection, and allowance of claims 1-11 and 24-26 are requested.

This supplemental amendment is accompanied by the filing of a *Request for Continued Examination (RCE)* under 37 C.F.R. §1.114.

The Amendment

In order to expedite prosecution of the application and advance the case toward allowance, the claims have been amended. No new matter was introduced by this amendment.

Claim 1 has been amended to specify that the method is used for continuous production of Hepatitis A virus (HAV) "antigen" and that HAV "antigen" is released into the medium. Support for this amendment can be found, for example, on page 5, paragraph [021] and page 10, paragraph [034].

Claim 10 has been amended to specify that the cells bound to the microcarrier continuously produce and release HAV "antigen" into the cell culture medium for at least 60 days. Support for this amendment can be found, for example, on page 18, paragraph [049] and paragraph [050].

Claims 24-26 have been added. Support for new claims 24 and 25 can be found in canceled claim 12 and, for example, on page 9, paragraphs [030], [031] and [032] and on page 19, paragraph [052], [053] and [054]. Support for new claim 26 can be found in canceled claim 21 and in paragraph [032] starting on page 9.

The Advisory Action

The Examiner indicates that the previously proposed amendments will be entered for purpose of appeal but they do not place the application into condition for allowance because the claims as amended allegedly fail to particularly point out and distinctly claim the subject matter and are, thus, rejected under 35 U.S.C. 112, second paragraph. It is allegedly unclear how the release of viral antigen into the cell culture medium is the cause of whole virus being released into the cell culture medium. The Examiner indicates that if the Applicant intends to claim that at least 50% of viral antigen is released into the medium, then the method preamble should be drawn to the production of HAV antigen. Further, the Examiner indicates that if the Applicant intends to claim that whole virus is released into the medium, then it is allegedly unclear how the release of viral antigens results in the release of whole virus since viruses are assembled inside cells.

The rejection is respectfully traversed to the extent that the rejection applies to the claims as amended.

Claim 1 has been amended to specify that the method is used for continuous production of Hepatitis A virus (HAV) "antigen" and that HAV "antigen" is released into the medium. Support for this amendment can be found, for example, on page 5, paragraph [021] and page 10, paragraph [034]. Claim 10, which depends on claim 1, has also been amended to specify that the cells bound to the microcarrier continuously produce and release HAV "antigen" into the cell culture medium for at least 60 days. Support for this amendment can be found on page 18, paragraph [049] and paragraph [050].

These amendments were made to place the claims into condition for allowance and should not be construed as an acquiescence in the rejection. The Applicants believe that these amendments comply with the Examiner's suggestion. However, the amendments do not change the meaning of the claims as they were previously presented.

For purpose of clarification, the present invention relates to the production of Hepatitis A virus (HAV) antigen, which can be HAV capsid proteins or other HAV particles. Paragraph [031] on page 9 of the specification indicates that a complete HAV particle means RNA-containing HAV particles of mature, infectious HAV virion particles which comprise capsid proteins VP1, VP2 and VP3, and immature provirions which contain VP1, VP3 and VP0 precursor polypeptides. The art generally considers an antigen to be a substance that is recognized as foreign by the immune system. Thus, one of skill would recognize that an HAV particle is an antigen. From this it is clear that the term *HAV antigen* encompasses HAV particles. In order to clarify this relationship, claim 12 has been canceled and new claims 24 and 25 have been added.

New claims 24 and 25 depend on claim 1 and are drawn to a *complete* Hepatitis A virus (HAV) particle and isolation thereof, respectively. As shown above, complete HAV particles are defined as RNA-containing HAV particles of mature, infectious HAV virion particles and/or immature provirions (*supra*). The method of claims 24 and 25 is described on page 9, paragraphs [030] through [033] and discussed in more detail in Example 7 on page 19. More specifically, Example 7 discusses purification of HAV antigen, wherein supernatant from the perfusion culture is collected and HAV antigen (continuously released into the medium) is separated from cellular debris. The concentrate is further purified and fractionated and each fraction is tested for HAV antigen (see paragraph [051]). The peak pool fractions 12-19 consist of mature virions and the peak pool fractions 22-25 contain provirions and/or preprovirions (see paragraph [052]). The respective fractions are then formulated into vaccine compositions (see paragraph [054]). Example 7 also states that this shows that by the process described, HAV is continuously released into cell culture medium by persistently infected VERO cells during large scale manufacturing (see paragraph [053]). Thus, isolation of mature HAV particles essentially also refers to isolation of HAV antigen. In light of the extensive description in the specification, the claims are clear and definite.

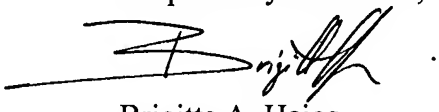
In light of the above amendments and remarks, Applicants respectfully request that the rejection of claims 1-11 under 35 U.S.C. 112, second paragraph, be withdrawn and the claims be placed into condition for allowance.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,



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Attachments
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